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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/837,886	04/18/2001	Stephen L. Mayo	A-65353-8/RFT/RMS/RMK	2783

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EXAMINER

KIM, YOUNG J

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 08/09/2002

3

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/837,886

Applicant(s)

MAYO ET AL.

Examiner

Young J. Kim

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-50 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 2-50 is/are rejected.
- 7) ☒ Claim(s) 4-20 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All, b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s) ____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2. 6) ☐ Other:

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DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has been assigned to Art Unit 1637. All further correspondence regarding this application should be directed to Group Art Unit 1637.

Claim Objections

Claims 4-20 are objected to because of the following informalities: claims 4-20 recite the limitation "claim 1." However, claim 1 had been canceled by the preliminary amendment filed with the instant application (filing date of April 18, 2001), rendering the claims lacking in proper antecedent basis.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-27, 29-48, and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-20, 29-48, and 50 recite the limitation "said protein." There is insufficient antecedent basis for this limitation in the claim. Amending the claim to recite, "said protein backbone" would overcome this rejection.

Claim 21 is indefinite for the recitation of the phrase, "known protein," because it becomes indefinite at which time frame and to whom the protein is considered to be known.

Claims 22-27 are indefinite because the claims do not have a conjunctive verb after the phrase, "protein backbone model," rendering the claims indefinite in what is included or excluded in/from the computer readable memory.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Hardman (U.S. Patent No. 4,939,666, issued July 3, 1990).

Claim 21 is drawn to a protein sequence is least about 5% different from a known protein sequence and is at least 20% more stable than the known protein sequence.

Claims 22-26 are drawn to a computer readable memory that comprise a side chain module to correlate a group of potential rotamers (or residues) for residue positions of a protein backbone and a ranking module that analyze the interaction of each of the rotamers with all or part of the remainder of the protein to generate a set of optimized protein sequences. Some embodiments are drawn to the analyzer module comprising van der Waals, atomic solvation, hydrogen bonding, or secondary structure scoring functions.

Hardman discloses a computerized method/algorithm that determines/predicts a protein's three-dimensional structure (Abstract, column 2). Hardman discloses that the properties of proteins depend directly from the protein's three-dimensional conformation and this

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conformation determines the activity or ability of enzymes, the capacity and specificity of binding proteins, and the structural attributes of receptor molecules, recognizing the need in the art for means to stabilize a protein's three-dimensional structure (column 2, lines 1-9).

Hardman discloses the method process that each residue in consideration must be globally optimized (minimization of total energy, column 10, lines 32-33) as well (column 12, lines 1-12, column 15, lines 50-68) wherein each of the peptide block (or residue in question, or potential rotamer), must be examined for at least several target parameters. Such parameters are disclosed as hydrogen bonding (claim limitation 25, column 38), van der Waals (claim limitation 23, column 39), atomic solvation (or hydration contribution, claim limitation 24, column 39), and Entropic contribution/Angle-dependent strain, i.e., steric hindrance (or secondary structure of claim 26, column 39).

Hardman also contemplates the substitution of residues in the existing structures to further optimize the structure (column 19, lines 1-22).

Hardman conducts the disclosed method through an algorithm on a computer, necessarily requiring a computer readable memory as evidenced throughout the disclosure.

Finally, Hardman discloses the production of the polypeptide produced by this method which would necessarily allow the generation of the claimed polypeptide.

According to *In re Best* 195 USPQ 430, 1997, the court stated that, "Patent Office can require applicant to prove that prior art products do not necessarily or inherently possess characteristics of his claimed product wherein claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes; burden of proof is on applicant" (pp. 430). Absent evidence that the disclosed method of Hardman

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cannot produce the polypeptide of the claimed, the method of Hardman and the polypeptide produced from said method would inherently anticipate the polypeptide of the claim.

Therefore, Hardman anticipates the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 22 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hardman (U.S. Patent No. 4,939,666, issued July 3, 1990) in view of Lee et al. (U.S. Patent No. 5,241, 470, issued August 31, 1993).

Claim 27 is drawn to the computer readable memory further comprising an assessment module to assess the correspondence between potential energy test results and theoretical potential energy data.

Hardman discloses a computerized method/algorithm that determines/predicts a protein's three-dimensional structure (Abstract, column 2). Hardman discloses that the properties of proteins depend directly from the protein's three-dimensional conformation and this conformation determines the activity or ability of enzymes, the capacity and specificity of binding proteins, and the structural attributes of receptor molecules, recognizing the need in the art for means to stabilize a protein's three-dimensional structure (column 2, lines 1-9).

Hardman discloses the method process that each residue in consideration must be globally optimized (minimization of total energy, column 10, lines 32-33) as well (column 12,

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lines 1-12, column 15, lines 50-68) wherein each of the peptide block (or residue in question, or potential rotamer), must be examined for at least several target parameters. Such parameters are disclosed as hydrogen bonding (claim limitation 25, column 38), van der Waals (claim limitation 23, column 39), atomic solvation (or hydration contribution, claim limitation 24, column 39), and Entropic contribution/Angle-dependent strain, i.e., steric hindrance (or secondary structure of claim 26, column 39).

Hardman also contemplates the substitution of residues in the existing structures to further optimize the structure (column 19, lines 1-22).

Hardman conducts the disclosed method through an algorithm on a computer, necessarily requiring a computer readable memory as evidenced throughout the disclosure.

Hardman does not disclose the comparison of the theoretical energy to the energy from the test data.

Lee et al. disclose a method of determining the packing conformation of amino acid side chains on a fixed peptide backbone wherein the side chains are "rotated" (thus rotamers) such that the side chains preferably settle in a low energy packing conformation (thus optimization) (Abstract, column 2, lines 1-25). Lee et al. also disclose that the conformation of energy of a peptide can be modified in many ways, ranging from potential energy functions having van der Waals, torsional biasing, electrostatic interaction, hydrogen bonding, hydrophobic interactions, entropic destabilization, cysteine bond formation, etc. (column 10, lines 54-61).

Lee et al. disclose that in order to test the reliability and consistency of the method, seven predictions for one protein was made and each of these predictions were compared to that of the native structure (column 25, line 68 to column 26, line 24).

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It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Hardman and Lee et al. to arrive at the invention as claimed. One of ordinary skill in the art would have been motivated to combine the teachings because by doing so, one of ordinary skill in the art would have been able to test the accuracy of the three-dimensional protein structure prediction as produced by Hardman. As the methods of Lee et al. and Hardman are directed in the art of protein structure predictions and optimization via computerized algorithm, one of ordinary skill in the art would have had a reasonable expectation of success at combining the accuracy/reliability step of Lee et al. into the method of Hardman to arrive at the invention as claimed.

Therefore, the invention as claimed is obvious over the cited references.

Double Patenting

Applicant is advised that should claims 2-20 be found allowable, claims 29-50 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claims are duplicative as illustrated below:

Claims 2-6 are duplicative to claims 29-33

Claim 7 is duplicative to claims 34, 49, and 50. Claims 49 and 50 includes all of the limitation of claim 7, thus identical in scope of the claims.

Claims 8-10 are duplicative to claims 35-37

Claims 11-20 are duplicative to claims 39-48

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A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 22-27 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 22-27 of copending Application No. 09/714,357. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. The claims of the instant application are identical to the copending application cited above.

Claims 2-5, 7-16, 28-32, 34-37, 39-44, 49, and 50 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-15 of prior U.S. Patent No. 6,188,965. This is a double patenting rejection.

Claims are identical in as follows:

Instant Application	U.S. Patent 6,188,965
Claims 2-5 and 29-32	Claims 2-5
Claim 28	Claim 1
Claims 7-16 and 34-37, 39-44, 49, and 50	Claims 6-15

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Claims 2, 6, 17-20, 28, 29, 33, 38, and 45-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 6, 11, and 18-21 of U.S. Patent No. 6,269,312. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reason.

The base claims 1 and 2 of the U.S. Patent 6,269,312 differs from the base claims 2, 28, and 29 (28 and 29 are duplicative claims as objected above) in that it recites an additional sub-step of altering at least one supersecondary structure parameter value of said protein backbone structure. However, the claims of the instant application are open to additional intervening step since the method "comprises" recited steps. Further, such modified step is considered to be a minor modification in the scope of the claims that is well within the purview of an ordinarily skilled in the art in the art of protein optimization. As for the dependent claims of the instant application, claims 6, 17-20, 28, 33, 38, and 45-48, they are identical to the dependent claims 6, 11, and 18-21 of the cited U.S. Patent.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (703) 308-9348. The Examiner can normally be reached from 8:30 a.m. to 7:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. The Fax number is (703) 746-

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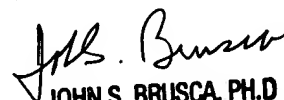
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3172. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Young J. Kim

7/31/02



JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER